





HoloMonitor® M4

Non-invasive Live Cell Analysis

The HoloMonitor® live cell imaging system enables long-term non-invasive analysis of cell cutures within your standard incubator. Cell biologists worldwide use PHI's label-free cell imager to automatically obtain live-cell morphology, migration, and proliferation data down to a single-cell level in real-time.

www.phiab.com





To understand and cure the diseases that still plague humanity, medical science needs new tools that gain widespread scientific use by being affordable to all scientists. Close to 20 years ago this, together with the excitement of working with something entirely new, inspired me and a group of engineers to start developing a technology that would allow cell biologists to non-invasively study cells while being cultured inside the incubator.

Sweden is the home of PHI, cinnamon buns, ABBA and technology innovations, including the three-point seat belt and mobile phones. But also Torbjörn Caspersson's cytophotometer, which led to the flow cytometer and eventually HoloMonitor®.

Rather surprisingly in hindsight, Caspersson's and other early cytometers in the 1930s where microscopy based. However, without digital image sensors and computer processing, the microscope was doomed to mainly remain a visual tool for cell biologists, while the flow cytometer developed to become its separate quantitative counterpart.

The cell, life's smallest building block, is fragile. Life is characterized by change. Science is unbiased observation and quantification. Technical developments associated with mobile phones have made it possible to unite these previously irreconcilable imperatives.

The HoloMonitor time-lapse cytometer is based on the successor of the soon 100-year-old phase-contrast microscope, and the technology employed has become known as quantitative phase imaging. Equipped with a digital image sensor, low power diode illumination and sophisticated computer algorithms, HoloMonitor quantifies living cells by measuring how light changes direction when passing through unstained cells. The cells are completely unaffected, as no light energy whatsoever is absorbed or transferred to the cells – no energy exchange, no change.

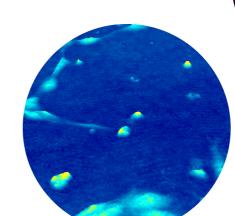
This allows HoloMonitor to gently image, quantify and over time monitor a large number of cells individually in their incubator environment, without the bias introduced by the harshness and toxicity of flow cytometry and fluorescent microscopy.

After all, Caspersson's original idea of microscopy-based cytometry wasn't so bad.

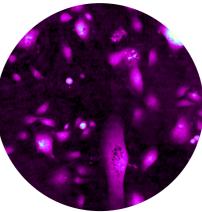


Peter Egelberg CEO and founder of PHI

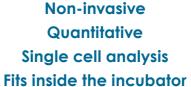
Focus on Your Cells

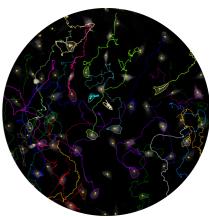


Induced pluripotent stem cells (iPS)

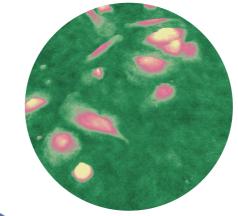


Primary human small airway epithelium cells (SAEC)

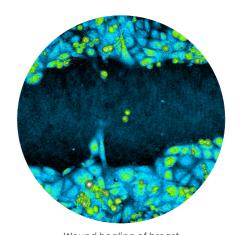




Single cell tracking



Macrophages



Wound healing of breast



HoloMonitor® is a live cell imaging system designed to visualize and quantify adherent cells over time. It is gentle to all cell types and can be used to monitor cell lines as well as delicate cell types, such as induced pluripotent stem cells or primary human cell cultures. As cell imaging with HoloMonitor is label–free and harmless to your cells, the cells can be used for further studies after imaging.

Our users have employed the system in a variety of fields, including cancer research, drug discovery or chemical toxicity studies. Research results are published in more than 200 peer – reviewed publications. All publications can be found on our website phiab.com.





User-friendly Applications

The HoloMonitor® software (App Suite) is a powerful tool designed to extract quantitative data about your cells from the holographic images captured by the instrument.

The App Suite software is intuitive and guides the user through the simple step—by—step work flow, from experiment setup to result analysis. You can also easily create colorful videos and images for peer-reviewed publications. All data can be exported to Excel for further analysis.

Guided End-point Assays

Ensure experiment reproducibility and optimal cell quality by checking up on your cells before setting up a timelapse experiment.



Evaluate cell integrity and detect changes of your cell culture.



CELL COUNTER

Determine the exact cell

number in your cell suspension.



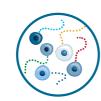
Guided Kinetic Assays

Tailored kinetic assays that automatically analyze images of your cells and provide kinetic data on your cell populations behavior in real-time.



DOSE RESPONSE ASSAY

Recognize drug toxicity patterns and kinetics of drug effects from interactive dose response curves.



CELL MOTILITY ASSAY

Explore average cell population motility based on cell speed and accumulated

cell distance in real-time



CELL PROLIFERATION ASSAY
Robust kinetic cell proliferation

Robust kinetic cell proliferation assessment by direct identification and counting of individual cells.



WOUND HEALING ASSAY
Easily obtain kinetic information on how

cell populations close the wound gap and determine cell front velocity.

In-depth Analysis

The single-cell tracking functionality enables in-depth analysis of both individual cells and entire cell populations at the same time.



SINGLE CELL TRACKING

Study single cell motility and migration patterns and distinguish between cell subpopulation behavior.



KINETIC MORPHOLOGY
Examine more than 30 parameters,

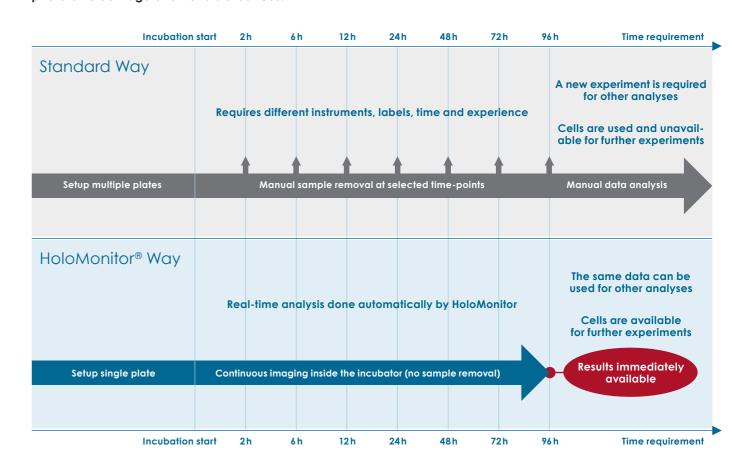
as cell morphology can be sensitive markers for cell damage.



Standard Way vs. HoloMonitor® Way

Standard cell culture methods require various instruments, from plate readers to microscopes. Experiments require multiple setups and consumables and most readouts are indirect as label intensities are measured.

HoloMonitor®, on the other hand, enables real-time label free and quantitative studies of your cells directly in the incubator. All information is directly obtained by monitoring cells without any phototoxic damage or other disturbances.



HoloMonitor® M4 Features

- Incubator tolerant design cells are kept undisturbed in their preferred environment during the entire experiment.
- Harmless laser illumination power enables long-term timelapse image acquisition and preserves your cell integrity.
- Motorized stage ensures precise multiple position imaging

 capturing the full story of your cells.
- Easy to use, powerful and unique software visualizes and provides quantitative data about your precious single cells or cell populations.
- Great image quality carefully designed vessel lids, HoloLids™, for perfect images.

HoloMonitor® M4 Benefits

- Save hands-on lab time, money and cells
- No expensive consumables or vessels needed
- Label-free technology with no phototoxicity
- Minimize user bias with automated analysis
- Monitor your cells 24/7 and get results in real-time
- Get direct and quantitative measurements
- Re-use your imaged cells further for other assays
- Re-analyze data for multiple results from one experiment

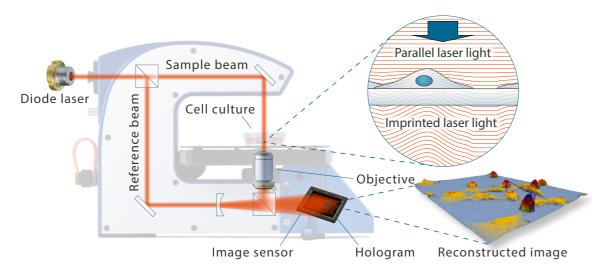
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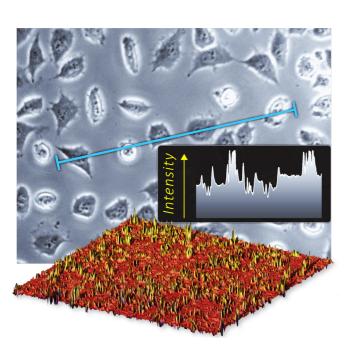
Defining Your Cells Without Labels

HoloMonitor® is based on quantitative phase imaging enabling non–invasive visualization and quantification of living cells without compromising cell integrity. Unlike phase contrast microscopy, individual cells can be identified using the HoloMonitor technology taking your research to new discovery horizons.



Holographic microscopy creates quantitative phase images by letting a sample beam and a reference beam interfere to generate an interference pattern – the hologram.

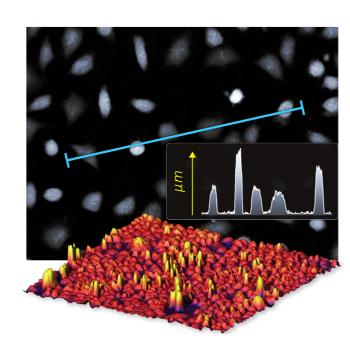
The hologram is recorded by an image sensor and processed by the computer to produce a reconstructed three dimensional (3D) image.



Phase Contrast Image

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- Using phase contrast, image background intensity values cannot be accurately determined.
- It is impossible to segment cells or display intensity as a 3D image.



Holographic Image

- · Holographic images have a background level of zero.
- It is easy to distinguish cells in the 3D quantitative phase image, as each single cell creates its own peak.

Technical Specifications

HoloMonitor® M4

Light source: External laser unit **Sample illumination:** 635 nm, 0.2 mW/cm²

Objective: 20x

Lateral resolution: 1 μm

Field of view: $567 \mu m \times 567 \mu m$ Working distance: 0.5 - 2 mm

Autofocusing range: 1.5mm
Image capture rate: 1 image/s

Image size: 1024×1024 pixels Stage travel range: $100 \times 70 \times 10$ (x×y×z)

Stage repeatability: 5µm

HoloMonitor® M4 dimensions: 290×200×190mm (w×d×h)

Space required in incubator: 400×270×190mm (w×d×h)

Weight: 5.15 kg

Computer Requirements

Operating system: Windows 10, 64-bit

Processor: Intel Core i7 (8th Gen)

Memory: 16 GB RAM (min 8 GB)

Hard drive: 512 GB SSD (min 256 GB)

Display: Full HD (min 1920×1080)

Other: 2 built–in USB ports

Sample and Environment

Cells: Adherent cell monolayer

Cell culture vessels*: 6-, 24-, 96-well, Petri, IBIDI

Operating temperature: 10-40°C
Operating humidity: Max 95%

For research use only.

* For information about recommended vessels please visit phiab.com/holomonitor/

holomonitor-system/

HoloMonitor® M4 Vessel Holders for Standard Cell Culture Vessels







4 Petri dishes simultaneously



3 microscopy slides simultaneously

HoloLids[™] for Superior Image Quality



35mm Petri dish



6-well plate



24-well plate



96-well plate

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